The pathogenesis of *C jejuni* infection more likely involves cytotoxin production or direct bacterial invasion and proliferation within the intestinal epithelium. Both natural and experimentally induced infections typically induce serum- and mucosal-specific antibody responses,[20] and the increased frequency of *C jejuni* bacteremia in persons with hypogammaglobulinemia[21,22] suggests that humoral responses play a key role in limiting the scope of infection. The increased frequency of chronic *C jejuni* infections in HIV-positive persons suggests, however, that cell-mediated immunity also may play a protective role.

Humoral immune responses also may have deleterious effects. Cross-reactivity between antibodies to *C jejuni* and host structures may be responsible for a number of other postinfectious illnesses including Reiter's syndrome and Guillain-Barré syndrome. Identifying particular serotypes or other strain characteristics capable of triggering this type of immune response is necessary so that control and prevention strategies may be devised.

In the past 20 years, *C jejuni* has become established as an important cause of enteric infection; the rheumatologic and neurologic sequelae of *C jejuni* infections also are becoming increasingly well publicized. But *C jejuni* infections continue to be underconsidered by physicians and underdiagnosed by microbiology laboratories, and cases are underreported. Despite the fact that campylobacters are detected in stool specimens of patients with diarrhea more frequently than *Salmonella* and *Shigella* species combined when they are looked for,[10] states continue to report cases of *C jejuni* infections at a far lower rate.[23,24] Further efforts are needed to increase campylobacter surveillance and to investigate the pathogenesis of the sequelae of campylobacter infections. Such studies are likely to shed light on the expanding roles these organisms play in causing human disease.

BAN MISHU, MD
MARTIN J. BLASER, MD
Department of Medicine
Division of Infectious Diseases
Vanderbilt University
School of Medicine
Department of Veterans Affairs
Medical Center
Nashville, Tennessee

REFERENCES

1. Peterson MC: Clinical aspects of *Campylobacter jejuni* infections in adults. West J Med 1994; 161:148-152

2. Kuroki S, Saida T, Nukina M, et al: *Campylobacter jejuni* strains from patients with Guillain-Barré syndrome belong mostly to Penner serogroup 19 and contain β-*N*-Acetylglucosamine. Ann Neurol 1993; 22:243-247

3. Mishu B, Amjad AA, Koski CL, et al: Serologic evidence of previous *Campylobacter jejuni* infection in patients with the Guillain-Barré syndrome. Ann Intern Med 1993; 118:947-953

4. Kaldor J, Speed BR: Guillain-Barré syndrome and *Campylobacter jejuni*. Br Med J 1984; 288:1867-1870

5. Blaser MJ, Olivares A, Taylor DN, Cornblath DR, McKhann GM: Campylobacter serology in patients with Chinese paralytic syndrome (Letter). Lancet 1991; 338:308

6. McKhann GM, Cornblath DR, Griffin JW, et al: Acute motor axonal neuropathy: A frequent cause of acute flaccid paralysis in China. Ann Neurol 1993; 33:333-342

7. Mishu B, Tauxe RV, Patton C: Clinical and epidemiologic features of non-*jejuni* campylobacters, *In* Nachamkin I, Blaser MJ, Tompkins LS (Eds): *Campylobacter jejuni*—Current Strategy and Future Trends. Washington, DC, American Society of Microbiology, 1992, pp 31-41

8. Lastovica AJ, Le Roux E: Prevalence and distribution of Campylobacter spp in the diarrhoeic stools and blood cultures of pediatric patients. Acta Gastroenterol Belg 1993; 56(suppl):34

9. Vandamme P, Falsen E, Rossau R, et al: Revision of *Campylobacter, Helicobacter*, and *Wolinella* taxonomy: Emendation of generic descriptions and proposal of *Arcobacter* gen nov. Int J Syst Bacteriol 1991; 41:88-103

10. Blaser MJ, Wells JG, Feldman RA, Pollard RA, Allen JR, The Collaborative Diarrhea Disease Study Group: *Campylobacter* enteritis in the United States: A multicenter study. Ann Intern Med 1983; 98:360-365

11. Sovillo FJ, Lieb LE, Waterman SH: Incidence of campylobacteriosis among patients with AIDS in Los Angeles County. J Acquir Immune Defic Syndr 1991; 4:598-602

12. Tauxe RV: Epidemiology of *Campylobacter jejuni* infections in the United States and other industrialized nations, *In* Nachamkin I, Blaser MJ, Tompkins LS (Eds): *Campylobacter jejuni*—Current Strategy and Future Trends. Washington, DC, American Society of Microbiology, 1992, pp 9-19

13. Surveillance of the Flow of Salmonella and Campylobacter in a Community. Seattle, Wash, Seattle-King County Department of Public Health, Communicable Disease Control Section, 1987

14. Deming MS, Tauxe RV, Blake PA, et al: Campylobacter enteritis at a university: Transmission from eating chicken and from cats. Am J Epidemiol 1987; 126:526-534

15. Perlman DM, Ampel NM, Schifman RB, et al: Persistent *Campylobacter jejuni* infections in patients infected with human immunodeficiency virus (HIV). Ann Intern Med 1988; 108:540-546

16. Bernard E, Roger PM, Carles D, Bonaldi V, Fournier JP, Dellamonica P: Diarrhea and *Campylobacter* infections in patients infected with the human immunodeficiency virus (Letter). J Infect Dis 1989; 159:143-144

17. Goossens H, Butzler JP, Takeda Y: Demonstration of cholera-like enterotoxin production by *Campylobacter jejuni*. FEMS Microbiol Lett 1985; 29:73-76

18. Lindblom GB, Johny M, Khalil K, Mazhar K, Ruiz-Palacios GM, Kaijser B: Enterotoxigenicity and frequency of *Campylobacter jejuni, C coli*, and *C laridis* in human and animal stool isolates from different countries. FEMS Microbiol Lett 1990; 54:163-168

19. Perez-Perez GI, Taylor DN, Echeverria PD, Blaser MJ: Lack of evidence of enterotoxin involvement in pathogenesis of Campylobacter diarrhea, *In* Nachamkin I, Blaser MJ, Tompkins LS (Eds): *Campylobacter jejuni*—Current Strategy and Future Trends. Washington, DC, American Society of Microbiology, 1992, pp 184-192

20. Black RE, Perlman D, Clements ML, Levine MM, Blaser MJ: Human volunteer studies with *Campylobacter jejuni*, *In* Nachamkin I, Blaser MJ, Tompkins LS (Eds): *Campylobacter jejuni*—Current Strategy and Future Trends. Washington, DC, American Society of Microbiology, 1992, pp 207-215

21. Johnson LJ, Nolan C, Wang SP, Shelton WR, Blaser MJ: Persistent *Campylobacter jejuni* infection in an immunocompromised patient. Ann Intern Med 1984; 100:832-834

22. Melamed J, Bujanover Y, Igra YS, Schwartz D, Zakuth V, Spirer Z: Campylobacter enteritis in normal and immunodeficient children. Am J Dis Child 1983; 137:752-753

23. Centers for Disease Control: Campylobacter Annual Tabulation, 1987-1989. Washington, DC, US Dept of Health and Human Services, Public Health Service, 1990

24. Centers for Disease Control: Salmonella isolates from humans in the United States, 1984-1986. MMWR CDC Surveill Summ 1988; 37:25-31

Are We Plumb Crazy?

LEAD (in Latin, *plumbum*) was used in some of the earliest inventions, including the forging of rigid metal implements, in medicinals, and in cosmetics. Its use was a key to the advancement of some civilizations and perhaps contributed to the demise of others.[1] Today lead lingers in the environment as an inauspicious consequence of human achievement. Had we known, in the making of that first leaded utensil, what poisonous course would be weaved for humankind, we may have tended our progress more cautiously. Yet in 1990, more than 1,275,000 metric tons of lead were used annually in the United States.

The toxicity of lead has been known since antiquity and was described by Nikander and other ancient writers. Premodern descriptions of lead toxicity focused only on occupational exposure. The classical clinical effects of lead and other metals were recognized in potters, painters, and miners. That it could afflict persons outside the trades was not reported until the late 1800s, however. The original cases of childhood lead poisoning due to lead-based paint were uncovered in Queensland, Australia, when paralysis, colic, convulsions, and optic neuritis were de-

scribed.[2] From this point on, it was clear that lead had become an environmental toxin. Cases of chronic nephritis that resulted from earlier childhood exposures were later described in the Queensland populations reported on by others. In the United States during the 1930s, increasing reports of urban childhood lead poisoning appeared. Despite the introduction of chelation therapy, morbidity and mortality remained high. In the 1960s mass screening programs revealed prevalences as high as 20% to 45% of children having blood lead concentrations greater than 40 μg per dl. In 1971, the Lead-Based Paint Prevention Act ordered the amount of lead in residential paints to be reduced to 0.06% following a Consumer Product Safety Commission study and also instructed the Office of Housing and Urban Development to study abatement measures. While new paint was to contain "safe" amounts of lead, the problem of lead in existing buildings began to perplex society.

The other major ubiquitous source of environmental lead was leaded gasoline. Although leaded gasoline had been manufactured and sold since 1923, rising blood lead concentrations and contamination of air and food convinced the Environmental Protection Agency to phase out lead in gasoline beginning in 1973. Societal and governmental recognition of increasing environmental exposure, leading to the regulation of lead in paints and gasoline, has resulted in a substantial reduction in exposure. Those of us growing up in the 1940s, 1950s, and 1960s had childhood daily doses and blood lead concentrations three to five times those of today's children. Indeed, most of the US urban population during those years would be judged lead "poisoned" by today's pediatric standard (>10 μg per dl). As blood levels have dropped with decreasing air and food concentrations, concern for lead-exposed persons has spread from medical and pediatric specialists to epidemiologists, public health officials, and preventive medicine physicians. The effects of lead exposure at today's environmental concentrations are insidious and subclinical, but still very real.

Elsewhere in this issue of the journal, Landrigan and Todd review the current understanding of lead exposure, its subtle effects, and newer public health issues.[3] The effect and magnitude of low levels of lead on neurobehavioral and cognitive functions in children are robust among both prospective and cross-sectional epidemiologic studies. Many possible confounding socioeconomic factors have been addressed. In individual persons, the assessment of neurobehavioral and cognitive impairment attributable to low levels of environmental lead is currently impossible because of a lack of simple measures, large individual variability, and multifactorial causes. Therefore, the screening of blood lead concentrations would lead to interventions that may ameliorate exposure and future effects. Blood lead screening is now mandated in many states, and many public health programs are following the guidelines provided by the Centers for Disease Control and Prevention (CDC). Iron deficiency produces strikingly similar neurobehavioral and cognitive effects in children, however.[4] Mild iron deficiency states have not been well studied, but may be prevalent in the same settings of lead exposure. Lead and iron interact environmentally, toxicokinetically, and toxicodynamically. For example, in low socioeconomic strata, decreased iron in the diet is likely to result in greater lead absorption and lead can compete with iron for ferrochelatase. It was recently shown that cognitive scores in children improved slightly after lead chelation and not after iron supplementation, but were significantly correlated with initial ferritin concentrations (about 40% were ferritin deficient) and not with initial lead concentrations.[5] These findings are consistent with either the known irreversible effects of iron deficiency on cognitive development or the earlier effect of lead. Although most of the major epidemiologic studies associating lead with neurobehavioral and cognitive outcomes have not examined iron stores as a covariate, an opportunity should not be missed in lead screening programs to prevent the possible irreversible effects of iron deficiency. Currently, the CDC recommends hemoglobin and iron measurements only as a follow-up evaluation to elevated blood lead concentrations. Initial testing is recommended.

Landrigan and Todd force us to consider some disturbing new questions regarding lead screening. Should every child in the United States be screened for blood lead concentrations of higher than 10 μg per dl, the current CDC recommended level of concern? Although a greater prevalence of elevated blood lead concentrations exists in inner-city children, many exposures are unique and site specific rather than environmentally ubiquitous. Herbal and traditional medicines, lead-glazed ceramic ware, lead-containing toys, molding and casting of lead in crafts and hobbies, and the renovation of old buildings in gentrified areas are some of the contemporary sources of pediatric lead poisoning. A number of screening programs have shown low prevalences of elevated blood lead levels in many suburban settings. For example, in Texas 8% of 43,436 children had blood lead concentrations of greater than 10 μg per dl and 0.8% had levels greater than 20 μg per dl. A more alarming prevalence was demonstrated in 4,196 inner-city children of Washington, DC, in which 18.6% had blood lead levels higher than 10 μg per dl and 1.6% higher than 25 μg per dl.[6,7] Given the variation in prevalence found for elevated blood lead levels in children, more focused screening will evolve as high-risk populations are identified. Screening and preventing exposure in populations at risk should continue because the long-term cost-effectiveness is likely to be greatest in the areas of educational and behavioral remediation.[8] Frontline health care professionals are often reluctant to carry out public health policies when they cannot see the fruits of their labors. Physicians can be encouraged to screen children if public health departments show how lead-induced disease and its interventions compare with other childhood illnesses. In essence, with feedback, health care workers will sense they are making a difference.

At what level do we stop worrying about lead? The balance of the cost-benefit equation is now changing somewhat as we confront possible and costly remedies.

Public health workers are recommending behavioral modification, dietary changes, repeated screening, and calcium and iron supplementation. While such recommendations have a good theoretical basis for their possible benefits and are considered precautionary and otherwise benign, outcomes research has yet to be done that establishes these interventions as efficacious. Abatement, though costly, is also a possible remedy. With the adoption of the Title X Lead-Based Paint Hazard Reduction Act of 1992, a $4 billion abatement industry has been launched. This industry will be highly regulated in that it creates a new occupational work exposure to be monitored by the Occupational Safety and Health Administration. Also, the disposal of the voluminous amounts of generated hazardous waste will be expensive. A recent randomized trial of soil and interior dust abatement showed modest declines in blood lead concentrations (about 2 μg per dl), but the authors concluded that such intervention would not produce substantial clinical or public health benefits.[9] On the other hand, abatement if done carelessly may reintroduce lead into a child's environment and reduce the efficacy of this intervention. If we wait for old houses containing lead paint to outlive their usefulness, what damage will be done to children in the interim? If we remove lead-contaminated paint now and bear the cost, how reliable, efficacious, and safe will this process be? Only limited studies exist. There is a great need for outcomes research on these topics.

Of great concern is that some practitioners are chelating at lower and lower blood lead concentrations. Standard chelation protocols have not been studied for their efficacy and long-term safety at blood lead concentrations of less than 45 μg per dl (one study is in progress), yet few alternative, effective, and economical interventions have been proved for blood lead concentrations in the 10- to 45-μg-per-dl range. The echo of "do no harm" looms over this approach. Recent work suggests that redistribution to other target organs may occur with several commonly used chelators.[10,11] Again, outcomes research on such interventions is needed.

One of the most important new developments in our understanding of lead toxicity, which is discussed by Landrigan and Todd, is the use of x-ray fluorescence of bone to determine lead content. With this new tool, we have a new measure of lead exposure or dose.[12] If a person had exposure to a constant amount of lead throughout their lifetime and internal exposure was well equilibrated with the deposition of lead in bone at all times, a blood concentration might be indicative of body burden or past exposure. Such is not the case, however. Lead exposure changes throughout our lifetime, and the physiologic processes that handle lead in the body change from infancy through old age. Therefore, blood lead concentrations tend to reflect recent exposure. Because a portion of all lead passing through the body is deposited in bones, the concentration in bone will represent a measure of lifetime exposure or "pass-through dose," an integrative measure of the amounts of lead seen by the soft tissue target organs. This has been validated in studies where inte-

grated measures of past exposure are shown to correlate well with bone lead levels as measured by x-ray fluorescence.[13] Because most of what we know about the effects of lead has been benchmarked to blood lead concentrations, a new view of lead's effects in relationship to bone concentrations will soon be available. In all likelihood, bone lead concentrations will be reflective of chronic injury to the central and peripheral nervous system, the kidneys, and the reproductive system. On the other hand, biologic processes with high turnover and repair (reversibility) are less likely to correlate with cumulative past lead exposure (hematologic, vasopressor, and gastrointestinal effects), where blood lead levels will remain indicative.

Landrigan and Todd question whether workplace standards of lead exposure need to be scrutinized and tightened. This, no doubt, will come to pass, particularly as scrutiny of the workplace and biologic monitoring become more convenient and practical. Currently, it is estimated that less than 10% of workplaces with lead exposures have effective surveillance programs. If blood lead testing were to become more convenient, both pediatric and occupational populations would benefit. The CDC is currently sponsoring cooperative agreements and grants to promote the development of portable blood lead testing devices. Landrigan and Todd suggest that the blood lead standard be lowered from 50 to 10 μg per dl. The foundation for this recommendation is the mismatch between 50 μg per dl and the much lower concentrations associated with lead effects; however, only the mild vasopressor effect of low blood lead concentrations in some populations would support a standard as low as 10 μg per dl. Lowering the standard to 10 μg per dl, however, is justified on the basis that workers should not have exposures that exceed the environmental background for the general population.

At least several million children may be at risk for some loss of their future cognitive potential, and more than a million workers are employed in lead-related jobs. Our body burdens of lead are still 100-fold higher than those of ancient peoples. Unfortunately, we assimilate our environment, and lead will always be present. Are we "plumb crazy"? As the effects of current body burdens are compared with future lower backgrounds, no doubt other effects of lead may be discernible.

JOHN OSTERLOH, MD
Associate Professor
Departments of Clinical Laboratory
Medicine and Medicine
University of California, San Francisco,
School of Medicine
San Francisco General Hospital

REFERENCES

1. Nriagu JO: Saturnine gout among Roman aristocrats—Did lead poisoning contribute to the fall of the empire? N Engl J Med 1983; 308:660-663

2. Gibson JL, Love W, Hardine D, Bancroft P, Turner AJ: Notes on lead poisoning as observed among children in Brisbane. Trans 3rd Intercolonial Med Congr 1892; 3:76-83

3. Landrigan PJ, Todd AC: Lead poisoning. West J Med 1994; 161:153-159

4. Lozoff B, Jimenez E, Wolf AW: Long-term developmental outcome of infants with iron deficiency. N Engl J Med 1991; 325:687-694

5. Ruff HA, Bijur PE, Markowitz M, Ma YC, Rosen JF: Declining blood lead levels and cognitive changes in moderately lead-poisoned children. JAMA 1993; 269:1641-1646

6. Hale TH, Douidar SM: Is routine blood lead screening in Texas children on Medicaid cost effective? Vet Hum Toxicol 1993; 35:354

7. Rifai N, Cohen G, Wolf M, et al: Incidence of lead poisoning in young children from inner-city, suburban, and rural communities. Ther Drug Monit 1993; 15:71-74

8. Matte T, Binder S: Cost and benefits of lead screening. JAMA 1993; 270:2054-2055

9. Weitzman M, Aschengrau A, Bellinger D, Jones R, Hamlin JS, Beiser A: Lead-contaminated soil abatement and urban children's blood lead levels. JAMA 1993; 269:1647-1654

10. Smith DR, Flegal AR: Stable isotopic tracers of lead mobilized by DMSA chelation in low lead-exposed rats. Toxicol Appl Pharmacol 1992; 116:85-91

11. Cory-Slechta DA, Weiss B, Cox C: Mobilization and redistribution of lead over the course of calcium disodium ethylenediamine tetraacetate chelation therapy. J Pharmacol Exp Ther 1987; 243:804-813

12. Kosnett MJ, Becker CE, Osterloh JD, Kelly TJ, Pasta DJ: Factors influencing bone lead concentration in a suburban community assessed by non-invasive K X-ray fluorescence. JAMA 1994; 271:197-203

13. Somervaille LJ, Nilsson U, Chettle DR, et al: In vivo measurements of bone lead—A comparison of two x-ray fluorescence techniques used at three different bone sites. Phys Med Biol 1989; 34:1833-1845

Office-Based Prevention—How Can We Make It Happen?

THE ARTICLE BY Dr James in this issue of the journal stimulates discussion about the best ways to encourage the use and delivery of clinical prevention services in office practice.[1] The author describes a computer-based method of enhancing prevention, sending yearly reminders to devote a visit to patient-appropriate prevention and screening activities. The prevention activities will be those deemed age- and gender-appropriate by one of several expert bodies,[2,3] with modifications based on patient and physician preferences.

How might such a method work in practice? That depends on whether patients and physicians want to practice prevention and on what they expect from their efforts. Physicians express general agreement with expert guidelines on prevention,[4,5] and patients say that they are willing to practice prevention.[6,7] Still, few preventive services are provided at the recommended levels. Only a third of women receive timely and appropriate breast cancer screening services, and about half to two thirds are appropriately screened for cervical cancer.[8-14] Of high-risk candidates for influenza, in any year only 20% receive immunization,[15] and only about half of all smokers report that they have ever been told to stop smoking or to smoke less by a physician.[16] Even among relatively affluent, well-insured children, only 45% of two-year-olds and 55% of six-year-olds are current for all recommended immunizations.[17] Other prevention services have similar or even lower rates of appropriate use.[11]

There are a variety of reasons for our failure to deliver prevention services, attributable to the physician, the patient, or the system in which the encounter occurs.[18] Time, both the patient's and the physician's, has been recognized as a barrier.[17-22] Physicians in a faculty adult primary care practice spent just 8% of their time in prevention, 60% of this in breast and cervical cancer screening and influenza immunization.[23] This brief period includes time spent in dedicated prevention visits and, more often, time borrowed during illness visits.

Attitudes of physicians and patients may also form barriers to prevention. Physicians and patients may find it difficult to justify expending time, money, and effort on preventing illness that seems unlikely or distant. Physicians who are not preventionists[24] by training may find remote outcomes or epidemiologically-based predictors unsatisfying.[24] Better personal health habits practiced by physicians have been shown, for male physicians, to lead to better prevention care for their patients.[25] The Women Physicians' Health Study, a study of the health and counseling practices of 10,000 women physicians being conducted by one of the authors (E.F.), should help clarify whether this is also true for women physicians.

Physicians may also forget to address prevention with their patients,[21] and applying risk profiles to the recommended schedules can make providing comprehensive prevention services even more complex. For example, the US Preventive Services Task Force (USPSTF) specifies 60 target conditions for prevention and 169 age- and gender-specific preventive services. One study used a computer-based algorithm of USPSTF rules based on age- and gender-specific risks to count an average of 24.5 recommendations for 230 adult ambulatory patients.[26] It is a difficult task to enumerate all appropriate recommendations and harder yet to complete them. Additionally, the logistics of prevention, such as the scheduling of mammograms, often done off-site from physicians' offices, provide further obstacles.

Physicians and patients may base decisions on patients' ability to pay or the availability of insurance reimbursement for preventive services.[13,22,27] Medicare, whose lead is often followed by private insurance companies, currently pays for only four preventive services: mammography, Pap smears, pneumococcal immunization, and hepatitis B immunization.[28] Hillary Rodham Clinton, in testimony to Congress about the Health Security Act, reported that she had to pay out-of-pocket for her last mammogram before her husband's inauguration. Even when physicians' and patients' knowledge, attitudes, and schedules allow for a preventive intervention to occur, restrictive and short-sighted financial policies may provide an enormous impediment to implementation.

Physicians have been overwhelmed with preventive guidelines, many conflicting,[7,29] and often are uncertain of appropriate screening schedules and procedures, leading some to underuse them. This may have changed,[30] however, with the publication of the USPSTF "Guidelines to Clinical Prevention Services" in 1989. That report, which included evidence-based recommendations and rankings of the effectiveness of available prevention services, has been widely disseminated. A new USPSTF report and the upcoming "Put Prevention Into Practice" campaign of the Department of Health and Human Services Office of Disease Prevention and Health Promotion may further improve physicians' knowledge about and confidence in the value of clinical prevention services.

How might an anniversary letter suggesting a prevention visit address these obstacles? A visit devoted solely to prevention and disease screening might relieve some of the time pressure felt by clinicians to work on established medical problems, though there is no guarantee that even